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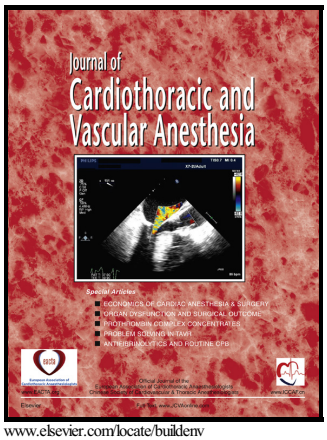
DOI:
10.1053/j.jvca.2017.09.033

Document Version
Peer reviewed version

Citation for published version (Harvard):
Yusuff, HO & Zochios, V 2017, 'Lactic Acidosis and Mitral Valve Surgery: Defining the relationship', *Journal of Cardiothoracic and Vascular Anesthesia*. https://doi.org/10.1053/j.jvca.2017.09.033



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Hakeem O. Yusuff, Vasileios Zochios

PII: S1053-0770(17)30772-3
DOI: http://dx.doi.org/10.1053/j.jvca.2017.09.033
Reference: YJCAN4347

To appear in: *Journal of Cardiothoracic and Vascular Anesthesia*

Cite this article as: Hakeem O. Yusuff and Vasileios Zochios, Lactic Acidosis and Mitral Valve Surgery: Defining the relationship, *Journal of Cardiothoracic and Vascular Anesthesia,* http://dx.doi.org/10.1053/j.jvca.2017.09.033

Type of contribution: Invited Editorial

Title: Lactic Acidosis and Mitral Valve Surgery: defining the relationship

Authors: [1]Hakeem O Yusuff MBBS, [2, 3] Vasileios Zochios MD

[1] University Hospitals of Leicester NHS Trust
Department of Cardiothoracic Anesthesia and Critical Care Medicine, Glenfield Hospital, Groby Road, Leicester, LE3 9QP, UK

[2] University Hospitals Birmingham NHS Foundation Trust
Department of Critical Care Medicine, Queen Elizabeth Hospital Birmingham, Edgbaston, Birmingham, B15 2WB, UK

[3] Perioperative Critical Care and Trauma Trials Group, Institute of Inflammation and Ageing Centre of Translational Inflammation Research, University of Birmingham, Birmingham, UK

Source of support: Nil

Conflicts of interest: Nil

Corresponding author:

Dr Vasileios Zochios MD
University Hospitals Birmingham NHS Foundation Trust
Department of Critical Care Medicine, Queen Elizabeth Hospital, Edgbaston, Birmingham, B15 2WB, UK
Perioperative Critical Care and Trauma Trials Group, Institute of Inflammation and Ageing Centre of Translational Inflammation Research
University of Birmingham, Birmingham, UK
Email: vasileioszochios@doctors.org.uk

EDITORIAL

Hyperlactatemia and lactic acidemia are common metabolic disorders after cardiac surgery with cardiopulmonary bypass. In this issue of the *Journal of Cardiothoracic and Vascular Anesthesia*, Mittnacht et al[1] sought to provide evidence through a retrospective data analysis that helps define the prognostic relationship between postoperative lactic acidosis and mitral valve surgery. The authors examined a clinical database from a cardiac surgery centre with a high volume caseload; however, being a retrospective study, bias cannot be eliminated. In addition, in view of the single centre status of the study the interpretation of these data has to be viewed in the context of other centre specific factors that would affect the results. However, the population analysed are sick cardiac surgical patients with a significant proportion with preoperative heart failure (41%), pulmonary hypertension (34%) and described as ASA physical status 3 and above (66%).

The imbalance between demand and supply at tissue level is ultimately viewed as the harbinger of organ dysfunction associated with high mortality. The origin of the process may differ however they lead to a common end point. The problem is that the point where this occurs is difficult to diagnose or detect and the likelihood of this happening depends on the physiological reserve of the patient to compensate for the pathophysiological insult. Serum lactate for a long time has been used as a surrogate marker to help detect this process with significant evidence indicating worse outcomes in patients with sepsis and other low flow states.[2] Cardiac surgery patients postoperatively can be ascribed to the latter. Blood lactate levels represent a balance between production and elimination and in cardiac surgery patients an increase in lactate can be attributed to factors increasing production and decreasing clearance e.g. hypothermia, postcardiotomy heart failure, inotrope use, postoperative acute kidney injury, acute liver dysfunction and blood transfusions.

However, there is a temporal relationship between the insult and measured blood lactate levels as the expectation is that a combination of patient reserve, restoration of normal physiology and critical care support with time should translate to lactate level returning to normal levels. Mittnacht et al[1] have specifically looked at analysing this specifically in patients having mitral valve surgery. The burden of mitral valve disease is very high with patients presenting with preoperative heart failure, pulmonary hypertension, right ventricular dysfunction and atrial fibrillation each of which independently predict mortality. It is expected that the pathophysiological insult of cardiopulmonary bypass is likely to be exacerbated in the context of mitral valve surgery hence these patients represent a target population to investigate.

The trend in postoperative lactate levels and mortality was investigated by Mak et al [3] in a single centre retrospective matched cohort analysis of cardiac surgical patients. Each patient with hyperlactemia was matched with two patients with normal lactate. Their results illustrated a relationship between the rate of rise of lactate and mortality, with non-survivors presenting with higher mean peak lactate and the mean time taken to peak was considerably longer (lactate – 11 mmol/l *vs* 3 mmol/l, time to peak – 37.6hours vs 7.5 hours). There is some congruency in the overall message of these two studies, however Mittnacht et al within the context of the mitral valve population have sought to qualify more precisely the interpretation of hyperlactemia. It is well established that lactate on arrival in the intensive care unit can be predictive of poor outcomes but how good it is as a predictor is difficult to ascertain. The authors recognised that significant hyperlactatemia on admission to intensive care unit occurred at a higher level (7 mmol/l) and this was associated with higher mortality. However, more than half of the patients that died did not have significantly high lactate levels

on admission. Therefore, the focus should be on the process and mechanisms causing the elevation of lactate. Irrespective of starting lactate, the continued rise of the lactate levels in the postoperative period despite support is probably indicative of the non-resolution of the supply demand substrate imbalance at tissue level that started whilst on cardiopulmonary bypass.

Epinephrine (adrenaline) was the first line inotrope to aid separation from cardiopulmonary bypass in accordance with local protocols. Epinephrine causes increased glycolysis and glycogenolysis in muscle leading to lactatemia.[4] This increase is often mild and transient however in the context of other factors it may contribute to significantly higher lactate levels seen on intensive care unit admission in the Mittnacht study. Given the retrospective nature of this study it is difficult to control for this confounder. Conversely, it is also possible to interpret the higher lactate levels on admission to be a reflection of the population studied as a significant proportion had mitral regurgitation as the primary pathology, heart failure and pulmonary hypertension.

In contrast to this, other studies have shown that lactate on admission is more predictive of mortality.[5] In a prospective analysis of 325 patients undergoing cardiac surgery with cardiopulmonary bypass, Maillet et al, sought to determine respective frequencies, risk factors, and outcomes of no hyperlactatemia, immediate hyperlactatemia (on admission to intensive care unit), or late hyperlactatemia after cardiac surgery. In this study all patients received normothermic cardiopulmonary bypass thus removing hypothermia as a factor in the etiogenesis of postoperative hyperlactatemia. Early hyperlactatemia was defined as an admission lactate of 3 mmol/l or more and interestingly a receiver operator characteristic (ROC) curve for lactate at 3 mmol/l and 5 mmol/l revealed that 3 mmol/l had the best balance

of specificity and sensitivity. Similarly, early and late hyperlactatemia predicted higher morbidity and mortality however early hyperlactatemia was more predictive. Factors contributing to late hyperlactatemia included hyperglycemia and adrenaline use. This suggests a disconnect between the intraoperative factors causing high lactate and the postoperative factors. In other words if a patient arrives in critical care unit with a normal lactate the assumption is that substrate imbalance that started on cardiopulmonary bypass has resolved and a late rise in lactate is probably due a new acquired process. If the intra-operative dysfunction has not resolved then the presenting lactate in the intensive care unit would be high and would probably continue to increase despite physiological support. Comparing the two studies, they have tried to identify the same population of patients whose outcomes are poor – patients with post-cardiopulmonary bypass low cardiac output state contributing to the substrate imbalance identified by hyperlactatemia. The study design by Maillet et al has the tendency to miss patients with an insidious clinical course who may present initially with normal lactate levels, which continue to increase in the postoperative period due to continuation of the intra/postoperative deranged physiology.

There is some congruency in all the evidence available on the factors contributing to hyperlactatemia in the postoperative period. Prolonged cardiopulmonary bypass and cross clamp times, use of adrenaline, preoperative atrial fibrillation and preoperative heart failure are associated with early and late postoperative hyperlactatemia. The pathogenesis of hyperlactatemia during cardiopulmonary bypass may be due to reduced tissue extraction. The reduction in perfusing pressure at the start of cardiopulmonary bypass contributes to this[6] and also the transition from pulsatile to non-pulsatile blood flow to the liver and kidneys (main organs for lactate clearance). [7] This effect is more pronounced with longer cardiopulmonary bypass and cross clamp times. When hypothermia is induced on bypass there is an increase in

serum lactate levels which resolves during rewarming and recent evidence suggests that in most patients this effect does not significantly contribute to postoperative hyperlactatemia. [8, 9]

Mittnacht and colleagues attempted to provide clarity on the best approach to interpretation of hyperlactatemia in patients undergoing mitral valve surgery. The retrospective nature of this study however weakens the strength of the evidence provided. It would be interesting to see if a prospective trial on a similar patient population with standardized perioperative management would yield the same results.

The evidence available on this subject emphasizes the prognostic value of postoperative hyperlactatemia. Importantly, hyperlactatemia (early or late) may be indicative of a group of patients who after cardiopulmonary bypass are unable to restore normal cardiac output or do so slowly. The consequent systemic and microcirculatory effects may increase the likelihood of major morbidity or mortality. Large-scale multicentre randomized controlled trials should test the hypothesis that lactate guided resuscitation and correction of hyperlactatemia in the context of high-risk cardiac surgery affects clinically important outcomes.

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